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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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HARRIET M. STRIMPEL; NEW ENGLAND BIOLABS, INC. 240 COUNTY ROAD IPSWICH, MA 01938-2723				
			EXAMINER STRZELECKA, TERESA E	
			ART UNIT 1637	PAPER NUMBER

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/665,633

Applicant(s)

KONG ET AL.

Examiner

Teresa E. Strzelecka

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-50 is/are pending in the application.
- 4a) Of the above claim(s) 14-28, 34-39 and 46-48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13, 29-33, 40-45, 49 and 50 is/are rejected.
- 7) ☒ Claim(s) 3 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. This office action is in response to an amendment filed August 18, 2006. Claims 1-50 were previously pending, with claims 14-28, 34-39 and 46-48 withdrawn from consideration. Applicants amended claims 1, 3-5, 31, 32 and 42. Claims 1-50 are pending, and claims 1-13, 29-33, 40-45, 49 and 50 will be examined.
2. Applicants' amendments overcame the following: rejection of claims 31 and 32 under 35 U.S.C. 112, second paragraph; rejection of claims 1-10, 13, 29 and 40-43 under 35 U.S.C. 102(b) as anticipated by Sninsky et al.; rejection of claims 1, 11-13, 31-33, 40-45 under 35 U.S.C. 102(e) as anticipated by Dean et al.; rejection of claim 30 under 35 U.S.C. 103(a) over Sninsky et al. All other previously presented objections and rejections are maintained for reasons given in the "Response to Arguments" below.
3. This office action contains new grounds for rejection necessitated by amendment.

Response to Arguments

4. Applicant's arguments filed August 18, 2006 have been fully considered but they are not persuasive.

A) Regarding the objection to claim 3 as not further limiting, Applicants argue that the amendment "wherein the target nucleic acid of step (a) is single stranded" now further limits claim 1. However, step (a) reads: "providing single strand templates of the target nucleic acid", therefore, the target nucleic acid of step (a) is already single stranded, making claim 3 not further limiting.

B) Regarding the rejection of claims 49 and 50 under 35 U.S.C. 102(e) as anticipated by Dean et al., Applicants argue that Dean et al. do not teach a helicase preparation comprising a single strand binding protein. However, no single strand binding protein is required by claim 49, since the term "helicase preparation", as defined on page 22, lines 2-7, does not require it:

“The helicase preparation refers to a mixture of reagents which when combined with a DNA polymerase, a nucleic acid template, four deoxynucleotide triphosphates, and primers are capable of achieving isothermal, exponential and specific nucleic acid amplification in vitro. “

The rejection is maintained.

Claim Objections

5. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 3 is not further limiting, as it contains the limitation “wherein the target nucleic acid of step (a) is a single-stranded nucleic acid”. This limitation is already present in step (a) of claim 1.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-13, 29-33, 40, 42 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Hogfree et al. (WO 01/09347).

Regarding claim 1, Hogfree et al. teach a method for exponentially and selectively amplifying a target nucleic acid, the method comprising:

(a) providing single strand templates of the target nucleic acid to be amplified (Hogfree et al. teach PCR reactions (page 45, third paragraph; page 46, page 47, first paragraph). Since the first step of a PCR reaction involves denaturing of target nucleic acid, Hogfree et al. inherently teach providing single strand templates of the target nucleic acid.);

(b) adding oligonucleotide primers for hybridizing to the templates of step (a) (Hogfree et al. teach PCR reactions (page 45, third paragraph; page 46, page 47, first paragraph), therefore they teach providing PCR primers.);

(c) synthesizing an extension product of the oligonucleotide primers which are complementary to the templates, by means of a DNA polymerase to form a duplex (Hogfree et al. teach PCR reactions (page 45, third paragraph; page 46, page 47, first paragraph), therefore they inherently teach producing duplex nucleic acid molecules.);

(d) contacting the duplex of step (c) with a helicase preparation for unwinding the duplex such that the helicase preparation comprises a helicase and a single strand binding protein (SSB) unless the helicase preparation comprises a thermostable helicase wherein the single strand binding protein is optional (Hogfree et al. teach adding a thermostable helicase to the PCR reactions (page 4, second paragraph; page 15, first paragraph; page 57, paragraphs 2-4; page 58, first and second paragraph).); and

(e) repeating steps (b)-(d) to exponentially and selectively amplify the target nucleic acid (Hogfree et al. teach selectively and exponentially amplifying the target (page 57, last paragraph; page 58, first and second paragraphs).).

Regarding claim 2, Hogfree et al. teach isothermal amplification (page 25, third paragraph).

Regarding claim 3, Hogfree et al. teach PCR reactions (page 45, third paragraph; page 46, page 47, first paragraph). Since the first step of a PCR reaction involves denaturing of target nucleic acid, Hogfree et al. inherently teach providing single strand templates of the target nucleic acid.

Regarding claim 4, Hogfree et al. teach DNA (page 4, fourth paragraph).

Regarding claim 5, Hogfree et al. teach RNA (page 4, fourth paragraph).

Regarding claim 6, Hogfree et al. teach PCR reactions (page 45, third paragraph; page 46, page 47, first paragraph), therefore they teach denaturation of double-stranded nucleic acid by heat.

Regarding claim 7, Hogfree et al. teach target nucleic acids with sizes from 0.5 kb to 30 kb (page 46, second paragraph), anticipating the range of about 50 bp to 100 kb.

Regarding claim 8, Hogfree et al. teach primer pairs hybridizing to the 5'-end and 3'-end of target nucleic acids (page 46, second paragraph; page 47, first paragraph).

Regarding claim 9, Hogfree et al. teach, for example, primers for amplification of 0.5 kb lac fragment (page 46, last line; page 47, first line). Both primers were 18 bp long, with 13 G/Cs and 5 A/Ts. According to a simple calculation where a melting temperature of a G-C pair is 4 °C and a melting temperature of an A-T pair is 2 °C, the melting temperature of the primers was: $13 \times 4\text{ °C} + 5 \times 2\text{ °C} = 62\text{ °C}$. Since the annealing temperature was 54 °C, the melting temperature of the primers was 8 °C above the annealing temperature, anticipating the value of about 10 °C, since Applicants did not define what range of values the term "about" corresponds to.

Regarding claims 10-12, Hogfree et al. teach Bst DNA polymerase (page 24, second paragraph).

Regarding claim 13, Hogfree et al. teach a preparation containing a single helicase (page 57, last paragraph).

Regarding claim 29, Hogfree et al. teach energy source being ATP (page 45, second paragraph; page 56, second paragraph).

Regarding claim 30, Hogfree et al. teach 5 mM ATP (page 45, second paragraph).

Regarding claims 31 and 32, Hogfree et al. teach single strand binding proteins (page 64, claim 1; page 65, claim 20; page 3, last paragraph; page 4, first paragraph). Applicants did not define what it means to be a "derivative" of the proteins in claim 32, therefore any single strand binding protein anticipates this limitation.

Regarding claim 33, Hogfree et al. teach accessory proteins (page 3, last paragraph; page 4, first paragraph).

Regarding claim 40, Hogfree et al. teach performing the PCR reaction annealing and extension steps at a substantially single temperature in the range of 20-75 C (page 47, first paragraph; amplification of 23 and 30-kb targets).

Regarding claim 42, Hogfree et al. teach performing the PCR reaction annealing and extension steps at about 60 C (page 47, first paragraph; amplification of 23 and 30-kb targets) and thermostable helicase (page 4, second paragraph; page 57, last paragraph).

Regarding claim 44, Hogfree et al. teach chromosomal DNA and sequencing (page 25, third paragraph; page 4, fourth paragraph).

8. Claims 1-8, 12, 13, 29, 31-33, 40, 41 and 43-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Armes et al. (US 2003/0219792 A1).

Regarding claim 1, Armes et al. teach a method for exponentially and selectively amplifying a target nucleic acid by:

(a) providing single strand templates of the target nucleic acid to be amplified (Armes et al. teach providing single-stranded target nucleic acid (page 3, [0026]));

(b) adding oligonucleotide primers for hybridizing to the templates of step (a) (Armes et al. teach adding primers (page 3, [0025]; page 5, [0043]; Fig. 1, 2).);

(c) synthesizing an extension product of the oligonucleotide primers which are complementary to the templates, by means of a DNA polymerase to form a duplex (Armes et al. teach synthesizing an extension product (Fig. 1, 2; page 5, 6, [0044]-[0047]));

(d) contacting the duplex of step (c) with a helicase preparation for unwinding the duplex such that the helicase preparation comprises a helicase and a single strand binding protein (SSB) unless the helicase preparation comprises a thermostable helicase wherein the single strand binding protein is optional (Armes et al. teach adding a helicase to the reactions which already contain a recA protein (page 3, [0031], page 4, [0033])); and

(e) repeating steps (b)-(d) to exponentially and selectively amplify the target nucleic acid (Armes et al. teach selectively and exponentially amplifying the target (page 6, [0049]; page 9, [0090], [0091])).

Regarding claim 2, Armes et al. teach isothermal amplification (page 12, [0117]).

Regarding claim 3, Armes et al. teach single-stranded target nucleic acid (page 3, [0026]).

Regarding claim 4, Armes et al. teach DNA (page 3, [0026]).

Regarding claim 5, Armes et al. teach RNA (page 3, [0026]).

Regarding claim 6, Armes et al. teach enzymatic denaturation of double-stranded nucleic acid (page 3, [0027]).

Regarding claim 7, Armes et al. teach amplification of DNA targets in the range of less than 1 kb to less than 500 megabases, anticipating the claimed range.

Regarding claim 8, Armes et al. teach using two primers, one of which hybridizes to the 3'-end and the other to the 5'-end of the target (Fig. 4, 6).

Regarding claim 12, Armes et al teach strand-displacing polymerase (page 3, 4 [0032]).

Regarding claim 13, Armes et al teach a single helicase (page 11, [0115]).

Regarding claim 29, Armes et al teach ATP (page 11, [0113]).

Regarding claim 31, Armes et al teach single-strand binding protein (Fig. 1, 2; page 11, [0115]).

Regarding claim 32, Armes et al. teach RecA (Fig. 1, 2), therefore, since Applicants did not define what it means to be a "derivative" of proteins of claim 32, RecA anticipates the claim.

Regarding claim 33, Armes et al teach accessory proteins (page 11, [0115]).

Regarding claims 40 and 41, Armes et al teach performing the reactions at a substantially single temperature between 20 and 75 °C and at about 37 °C (page 12, [0117]).

Regarding claim 43, Armes et al teach detection of pathogens (page 12, 13 [0125]).

Regarding claims 44 and 45, Armes et al teach detecting sequence variations in genomic DNA (page 12, [0118]-[0124]).

9. Claims 49 and 50 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al. (U.S. Patent No. 6,977,148 B2; cited in the previous office action).

Regarding claim 49, Dean et al. teach an assay for helicase, the assay comprising:

(a) preparing a helicase preparation comprising the helicase, an NTP or dNTP, a buffer, wherein the buffer has a pH in the range of about pH 6.0- 9.0, a concentration of NaCl or KCl in a concentration range of 0-200mM, and Tris-acetate or Tris-HCl and optionally one or more of a single stranded binding protein and an accessory protein (col. 24, lines 16-49; col. 36, lines 24-51);

Art Unit: 1637

(b) adding a target nucleic acid, oligonucleotide primers, four dNTPS and a DNA polymerase to the helicase preparation (col. 24, lines 16-49; col. 36, lines 24-51);

(c) incubating the mixture at a temperature between about 20 C and 75 C (col. 24, lines 36-49); and

(d) analyzing the DNA on an agarose gel to determine whether selective and exponential amplification has occurred (col. 36, lines 24-51).

Regarding claim 50, Dean et al. teach varying the temperature (col. 24, lines 36-49) and time of incubation (col. 38, lines 49-65).

10. No claims are allowed.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

Art Unit: 1637

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
10/26/06